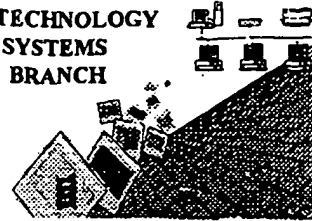


BIOTECHNOLOGY
SYSTEMS
BRANCH



RAW SEQUENCE LISTING
ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: 09/643,128
Source: 622
Date Processed by STIC: 11/21/03

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.

PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:

- 1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,
- 2) TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY

FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 703-308-4212; FAX: 703-308-4221

Effective 12/13/03: TELEPHONE: 571-272-2510; FAX: 571-273-0221

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE **CHECKER VERSION 4.1 PROGRAM**, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:

<http://www.uspto.gov/web/offices/pac/checker/chkr41note.htm>

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.

Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.

Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:

1. EFS-Bio (<<http://www.uspto.gov/ebc/efs/downloads/documents.htm>> , EFS Submission User Manual - cPAVE)
2. U.S. Postal Service: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
3. Hand Carry directly to (EFFECTIVE 12/01/03):
U.S. Patent and Trademark Office, Box Sequence, Customer Window, Lobby, Room 1B03, Crystal Plaza Two, 2011 South Clark Place, Arlington, VA 22202
4. Federal Express, United Parcel Service, or other delivery service to: U.S. Patent and Trademark Office, Box Sequence, Room 4B03-Mailroom, Crystal Plaza Two, 2011 South Clark Place, Arlington, VA 22202

Revised 10/08/03

Raw Sequence Listing Error Summary

ERROR DETECTED	SUGGESTED CORRECTION	SERIAL NUMBER: <u>09/643,128</u>
ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE.		
1. <u> </u> Wrapped Nucleics Wrapped Aminos	The number/text at the end of each line "wrapped" down to the next line. This may occur if your file was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will prevent "wrapping."	
2. <u> </u> Invalid Line Length	The rules require that a line not exceed 72 characters in length. This includes white spaces.	
3. <u> </u> Misaligned Amino Numbering	The numbering under each 5 th amino acid is misaligned. Do not use tab codes between numbers; use space characters, instead.	
4. <u> </u> Non-ASCII	The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please ensure your subsequent submission is saved in ASCII text.	
5. <u> </u> Variable Length	Sequence(s) <u> </u> contain n's or Xaa's representing more than one residue. Per Sequence Rules, each n or Xaa can only represent a single residue. Please present the maximum number of each residue having variable length and indicate in the <220>-<223> section that some may be missing.	
6. <u> </u> PatentIn 2.0 "bug"	A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid sequence(s) <u> </u> . Normally, PatentIn would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence. This applies to the mandatory <220>-<223> sections for Artificial or Unknown sequences.	
7. <u> </u> Skipped Sequences (OLD RULES)	Sequence(s) <u> </u> missing. If intentional, please insert the following lines for each skipped sequence: (2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown) (i) SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading) (xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown) This sequence is intentionally skipped Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences.	
8. <u> </u> Skipped Sequences (NEW RULES)	Sequence(s) <u> </u> missing. If intentional, please insert the following lines for each skipped sequence. <210> sequence id number <400> sequence id number 000	
9. <u> </u> Use of n's or Xaa's (NEW RULES)	Use of n's and/or Xaa's have been detected in the Sequence Listing. Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present. In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents.	
10. <u> </u> Invalid <213> Response	Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or is Artificial Sequence	
11. <u> </u> Use of <220>	Sequence(s) <u> </u> missing the <220> "Feature" and associated numeric identifiers and responses. Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or "Unknown." Please explain source of genetic material in <220> to <223> section. (See "Federal Register," 0001/1998, Vol. 63, No. 104, pp. 29631-32) (Sec. 1.823 of Sequence Rules)	
12. <u> </u> PatentIn 2.0 "bug"	Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.	
13. <u> </u> Misuse of n/Xaa	"n" can only represent a single <u>nucleotide</u> ; "Xaa" can only represent a single <u>amino acid</u>	



IFW16

RAW SEQUENCE LISTING
PATENT APPLICATION: US/09/643,128

DATE: 11/21/2003
TIME: 11:01:32

Input Set : A:\PTO.YF.txt
Output Set: N:\CRF4\11212003\I643128.raw

4 <110> APPLICANT: Jifan Hu, GMR Epigenetics Corporation;
5 Andrew R. Hoffman, Stanford University
7 <120> TITLE OF INVENTION: Gene Inactivation by Targeted DNA Methylation
9 <130> FILE REFERENCE: 10853-005-999
C--> 11 <140> CURRENT APPLICATION NUMBER: US/09/643,128
12 <141> CURRENT FILING DATE: 2000-08-21
14 <150> PRIOR APPLICATION NUMBER: US60/96,749
15 <151> PRIOR FILING DATE: 2000-04-12
17 <160> NUMBER OF SEQ ID NOS: 56
19 <170> SOFTWARE: PatentIn For Windows v. 3

Global error.
Consult Sequence Rules.
Consult sample Sequence Listing
sample (attached)
pp 1-5

ERRORED SEQUENCES

21 <210> SEQ ID NO: 1
22 <211> LENGTH: 5
23 <212> TYPE: DNA
24 <213> ORGANISM: Artificial sequence
W--> 26 <220> FEATURE: Hairpin *this belongs on <223> line. Never insert a response to <220> it is a "header" only.*
W--> 27 <221> NAME/KEY: m5C
28 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-methylcytidine (m5C) at CpG
29 dinucleotide sequence
31 <400> SEQUENCE: 1
E--> 32 m5cgfm5cg *delete "m5" - show nucleotide only*
36 <210> SEQ ID NO: 2
37 <211> LENGTH: 5
38 <212> TYPE: DNA
39 <213> ORGANISM: Artificial sequence
W--> 41 <220> FEATURE: Hairpin *Same error*
W--> 42 <221> NAME/KEY: m5C
43 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-methylcytidine (m5C) at CpG
44 dinucleotide sequence
46 <400> SEQUENCE: 2
E--> 47 m5cgfm5cg *it needs explanation in <220>-<223> section. (see item 9 on Error summary sheet)*
51 <210> SEQ ID NO: 3
52 <211> LENGTH: 10
53 <212> TYPE: DNA
54 <213> ORGANISM: Artificial sequence
W--> 56 <220> FEATURE: Hairpin
W--> 57 <221> NAME/KEY: m5C
58 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-methylcytidine (m5C) at CpG

59 dinucleotide sequence
61 <400> SEQUENCE: 3

RAW SEQUENCE LISTING

DATE: 11/21/2003

PATENT APPLICATION: US/09/643,128

TIME: 11:01:32

Input Set : A:\PTO.YF.txt

Output Set: N:\CRF4\11212003\I643128.raw

do not show dashes

E--> 62 cgacg~~m5cg~~m5cg
 66 <210> SEQ ID NO: 4
 67 <211> LENGTH: 22
 68 <212> TYPE: DNA
 69 <213> ORGANISM: Artificial sequence

W--> 71 <220> FEATURE: Hairpin

W--> 72 <221> NAME/KEY: m5C

73 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-methylcytidine (m5C) at CpG

74 dinucleotide sequence

76 <300> PUBLICATION INFORMATION:

77 <301> AUTHORS: Xiaoming Yao, Ji-Fan Hu, Mark Daniels, Hadas Shiran, Xiangjun Zhou, Huifan

78 Yan,
 79 Hongqi Lu, Zhilan Zeng, Qingxue Wang, Tao Li, and Andrew R. Hoffman

80 <302> TITLE: A methylated oligonucleotide inhibits IGF2 expression and enhances survival in a model of hepatocellular carcinoma

83 <303> JOURNAL: Journal of Clinical Investigation

W--> 84 <307> DATE: in press

86 <400> SEQUENCE: 4

E--> 87 agccm5cg~~m5cg~~m5cgaggagtm5cg
 91 <210> SEQ ID NO: 5
 92 <211> LENGTH: 33
 93 <212> TYPE: DNA
 94 <213> ORGANISM: Artificial sequence

W--> 96 <220> FEATURE: Hairpin

W--> 97 <221> NAME/KEY: m5C

98 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-methylcytidine (m5C) at CpG

99 dinucleotide sequence

101 <300> PUBLICATION INFORMATION:

102 <301> AUTHORS: Xiaoming Yao, Ji-Fan Hu, Mark Daniels, Hadas Shiran, Xiangjun Zhou, Huifan

103 Yan,
 104 Hongqi Lu, Zhilan Zeng, Qingxue Wang, Tao Li, and Andrew R. Hoffman

105 <302> TITLE: A methylated oligonucleotide inhibits IGF2 expression and enhances survival in a model of hepatocellular carcinoma

108 <303> JOURNAL: Journal of Clinical Investigation

W--> 109 <307> DATE: in press

111 <400> SEQUENCE: 6

E--> 112 cgacg~~m5cg~~m5cgagccm5cg~~m5cg~~m5cgaggagtm5cg
 116 <210> SEQ ID NO: 6
 117 <211> LENGTH: 22
 118 <212> TYPE: DNA
 119 <213> ORGANISM: Artificial sequence

121 <220> FEATURE:

W--> 122 <221> NAME/KEY:

123 <223> OTHER INFORMATION: Phosphothioate oligonucleotide

125 <300> PUBLICATION INFORMATION:

126 <301> AUTHORS: Xiaoming Yao, Ji-Fan Hu, Mark Daniels, Hadas Shiran, Xiangjun Zhou, Huifan

group all nucleotides into 10's, with a space between each group

22< insert cumulative base total at right margin of each line

group into 10's

33<

127 Yan,

RAW SEQUENCE LISTING

PATENT APPLICATION: US/09/643,128

DATE: 11/21/2003

TIME: 11:01:32

Input Set : A:\PTO.YF.txt

Output Set: N:\CRF4\11212003\I643128.raw

128 Hongqi Lu, Zhilan Zeng, Qingxue Wang, Tao Li, and Andrew R. Hoffman
 129 <302> TITLE: A methylated oligonucleotide inhibits IGF2 expression and enhances
 130 survival
 131 in a model of hepatocellular carcinoma
 132 <303> JOURNAL: Journal of Clinical Investigation
 W--> 133 <307> DATE: in press group into 10's
 135 <400> SEQUENCE: 6 21< insert
 E--> 136 ggtcacgggtcagggcgtatggt
 140 <210> SEQ ID NO: 7
 141 <211> LENGTH: 21
 142 <212> TYPE: DNA
 143 <213> ORGANISM: Artificial sequence, (c-myc) this goes on <2237> line.
 W--> 145 <220> FEATURE: Hairpin Do not insert explanation on
 W--> 146 <221> NAME/KEY: m5C <2137> line.
 147 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-
 methylcytidine (m5C) at CpG
 148 dinucleotide sequence
 150 <400> SEQUENCE: 7 group into 10's
 E--> 151 tm5cgctaatctcm5cgcccaom5cgg 21<
 154 <210> SEQ ID NO: 8
 155 <211> LENGTH: 20
 156 <212> TYPE: DNA
 157 <213> ORGANISM: Artificial sequence, (c-myc)
 W--> 159 <220> FEATURE: Hairpin
 W--> 160 <221> NAME/KEY: m5C
 161 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-
 methylcytidine (m5C) at CpG
 162 dinucleotide sequence group into 10's
 164 <400> SEQUENCE: 8 20<
 E--> 165 acm5cgccctttataatcm5cga
 169 <210> SEQ ID NO: 9
 170 <211> LENGTH: 20
 171 <212> TYPE: DNA
 172 <213> ORGANISM: Artificial sequence, (c-myc)
 W--> 174 <220> FEATURE: Hairpin
 W--> 175 <221> NAME/KEY: m5C
 176 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-
 methylcytidine (m5C) at CpG
 177 dinucleotide sequence 10's
 179 <400> SEQUENCE: 9 20<
 E--> 180 tcm5cgcccaom5cgccctttat
 184 <210> SEQ ID NO: 10
 185 <211> LENGTH: 18
 186 <212> TYPE: DNA
 187 <213> ORGANISM: Artificial sequence, HIV
 W--> 189 <220> FEATURE: Hairpin
 W--> 190 <221> NAME/KEY: m5C
 191 <223> OTHER INFORMATION: Phosphothioate oligonucleotide modified with 5-
 methylcytidine (m5C) at CpG
 192 dinucleotide sequence 10's
 194 <400> SEQUENCE: 10 18<
 E--> 195 cam5cgtagcmm5cgagagm5ctg FYI
 199 <210> SEQ ID NO: 11

The
the
sequence
FYI
The sequence is throughout
the sequence and contains
several errors

IMPORTANT

<110> Smith, John; Smithgene Inc.

<120> Example of a Sequence Listing

<130> 01-00001

<140> PCT/EP98/00001
<141> 1998-12-31

<150> US 08/999,999
<151> 1997-10-15

<160>

<170> Patent in version 2.0

<210> 1
<211> 389
<212> DNA
<213> Paramecium sp.

<220>
<221> CDS
<222> (279)... (389)

<300>
<301> Doc. Richard
<302> Isolation and Characterization of a Gene Encoding a
Protease from Paramecium sp
<303> Journal of Genes
<304> 1
<305> 4
<306> 1-7
<307> 1988-06-31
<308> 123456
<309> 1988-06-31

<400>	1						60
agcagcagc	atccctgctg	ccctctctct	ctgggctct	cacctgct	atcagatctc		
							120
agggagagc	ctctgacct	ccctgctct	ctcagctct	caggcaggc	ggcaggcagc		
							180
ctgctgctc	atctgctgca	gtgctcagc	ctctcagct	agcctcagg	ctggctccgc		
							240
cgcggcgcg	cggccctct	cgcgctctc	ctcgcctct	ctctgctct	ctctcgcct		

Consult

Appendix 3, page 2

```

ggaccctgall  aggtgagcag  gaaggaggggg  cagcttagc  296
Met Val Ser Met Phe Ser
1 5

ttg tct ttc aaa tgg cct gga ttt tgt ttg bct gtt tgt ttg ttc coa 344
Leu Ser Phe Lys Trp Pro Gly Phe Cys Leu Phe Val Cys Leu Phe Cln
10 15 20

tgt ccc aaa gtc ttc ccc tgt cag tca tca ctg cag ccg aat ctt 389
Cys Pro Lys Val Leu Pro Cys His Ser Ser Leu Gln Pro Asn Leu
25 30 35

```

<210> 2
 <211> 37
 <212> PRT
 <213> Paramecium sp.

```

<<00> 2
Met Val Ser Met Phe Ser Leu Ser Phe Lys Trp Pro Gly Phe Cys Leu
1 5 10

Phe Val Cys Leu Phe Gln Cys Pro Lys Val Leu Pro Cys His Ser Ser
20 25 30

Leu Gln Pro Asn Leu
35

```

<210> 3
 <211> 11
 <212> PRT
 <213> Artificial Sequence

<220>
 <221> Designed peptide based on size and polarity to act as a linker between the alpha and beta chains of Protein XYZ.

```

<<00> 3
Met Val Asn Leu Glu Pro Met His Thr Glu Ile
1 5 10

```

<210> 4
 <400> 4
 000

[Annex VIII follows]

identifiers and their accompanying information as shown in the following table. The numeric identifier shall be used only in the "Sequence Listing." The order and presentation of the items of information in the "Sequence Listing" shall conform to the arrangement given below. Each item of information shall begin on a new line and shall begin with the numeric identifier enclosed in angle brackets as shown. The submission of those items of information designated with an "M" is mandatory. The submission of those items of information designated with an "O" is optional. Numeric identifiers <110> through <170> shall only be set forth at the beginning of the "Sequence Listing." The following table illustrates the numeric identifiers.

Numeric Identifier	Definition	Comments and Format	Mandatory (M) or Optional (O)
<110>	Applicant	Preferably max. of 10 names; one name per line; preferable format: Surname, Other Names and/or Initials	M
<120>	Title of Invention		M
<130>	File Reference	Personal file reference	M, when filed prior to assignment of appl. number
<140>	Current Application Number	Specify as: US 07/999,999 or PCT/US96/99999	M, if available
<141>	Current Filing Date	Specify as: yyyy-mm-dd	M, if available
<150>	Prior Application Number	Specify as: US 07/999,999 or PCT/US96/99999	M, if applicable include priority documents under 35 USC 119 and 120
<151>	Prior Application Filing Date	Specify as: yyyy-mm-dd	M, if applicable
<160>	Number of SEQ ID NOs	Count includes total number of SEQ ID NOs	M
<170>	Software	Name of software used to create the Sequence Listing	O
<210>	SEQ ID NO: #:	Response shall be an integer representing the SEQ ID NO shown	M
<211>	Length	Respond with an integer expressing the number of bases or amino acid residues	M

<212>	Type	Whether presented sequence molecule is DNA, RNA, or PRT (protein). If a nucleotide sequence contains both DNA and RNA fragments, the type shall be "DNA." In addition, the combined DNA/RNA molecule shall be further described in the <220> to <223> feature section.	M
<213>	Organism	Scientific name, i.e. Genus/species, Unknown or Artificial Sequence. In addition, the "Unknown" or "Artificial Sequence" organisms shall be further described in the <220> to <223> feature section.	M
<220>	Feature	Leave blank after <220>. <221-223> provide for a description of points of biological significance in the sequence.	M, under the following conditions: if "n," "Xaa," or a modified or unusual L-amino acid or modified base was used in a sequence; if ORGANISM is "Artificial Sequence" or "Unknown," molecule is combined DNA/RNA.
<221>	Name/Key	Provide appropriate identifier for feature, preferably from WIPO Standard ST. 25 (1998), Appendix 2, Tables 5 and 6	M, under the following conditions: if "n," "Xaa," or a modified or unusual L-amino acid or modified base was used in a sequence
<222>	Location	Specify location within sequence; where appropriate state number of first and last bases/amino acids	M, under the following conditions: if "n," "Xaa," or a modified or unusual L-amino acid or modified